普康
PUKANG

PRODUCT MANUAL

Sichuan Pukang Pharmaceutical Co.Ltd.

Factory Address: No.36 Chuang Xin Road, Yuechi County Economic Development Zone, Guang' an, Sichuan Province.

Chengdu Pukang Biotechnology Co., Ltd.

R&D Address:
Building 3, Jindi Weixin Wenjiang Zhizao Park Area, No. 88 Haida Road, Wenjiang District, Chengdu City.
Tel: +86-28-63976226
Email: export@pu-kang.com sale@pu-kang.com
Website: www.pu-kang.com

PUKANG
BIOTECHNOLOGY 普康生物科技

普康
PUKANG

OUR MISSION

Developing Biologics
Longer-Acting

OUR PHILOSOPHY

Quality First, Innovation First, People Oriented, Integrity Rooted

COMPANY PROFILE

Chengdu Pukang Biotechnology Co., Ltd., established in 2008, is a high-tech enterprise pioneering in China in the field of long-acting peptide drug modification technologies. Pukang has provided a diverse range of structurally novel, high-quality modifiers to over 200 well-known global pharmaceutical companies (including global TOP 20 pharma enterprises). These products assist clients in rapidly enabling innovative peptide drug molecule screening and evaluation. Pukang has completed the full-process development of side chains for drugs like Semaglutide and Tirzepatide, also provide the DMF documents of products, supporting multiple pharmaceutical companies in their New Drug Application (NDA) submissions. Products from several clients have entered Phase III clinical trials, with some initiating production registration processes. The DMF registration for the Semaglutide API by overseas client received zero deficiency for the side chain documentation.

The company has built 6,000m² of trial lab, 3,000m² of pilot lab, and 60,000m² of production base on the requirements of GMP and ICH Q7. The R&D base and industrialization base are all in accordance with the international advanced concepts and regulations, and Pukang has set up improved the quality management system and EHS management system, to ensure the stable supply and satisfy the needs of downstream customers from the R&D of the new drug project to the industrialization of the whole stage.

Industrialization advantages of Pukang:

- Reactor scale range: 100L to 5,000L
- Reaction temperature range: -20°C to 200°C
- Current annual side chain capacity: 5 tons (Phase II will be put into production in 2026, designed capacity: 30 tons)
- Comprehensive QMS and EHS Management System

PUKANG
BIOTECHNOLOGY 普康生物科技

普康 PUKANG

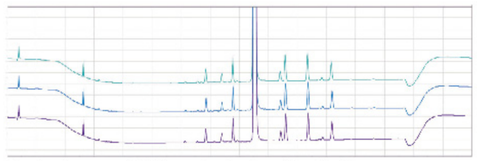
PEPTIDE LONG-ACTING SIDE-CHAIN TECHNOLOGY PLATFORM

External modification of side chain is one of the important technologies for long-acting peptides. Pukang has established a peptide long-acting modification platform to provide multiple varieties of modified side chains and side chain fragments, which helps drug development and accelerates the industrialization of pharmaceutical.

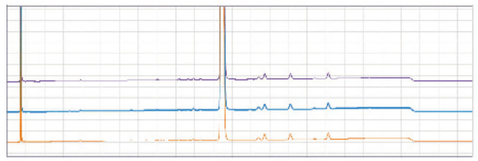
LONG-ACTING PEPTIDE SIDE CHAIN VARIETIES:

1、Semaglutide side chain (DMF Filing No.039906)
2、Tirzepatide side chain (DMF Filing No. 039989)
3、Insulin Degludec side chain
4、Icodec insulin side chain
5、Liraglutide side chain
6、Long-acting growth hormone side chain
7、Retatrutide side chain
8、Survodutide side chain
9、Mazdutide side chain
10、Bofenglutide side chain
11、Other customized sidechains and their blocks

Side-chain modifiers are one of the important factors in the pharmacokinetic behavior of peptide products. The development and production of side-chain modifiers of Pukang are carried out in accordance with the requirements of ICH Q11 and other relevant guidelines. According to its structural characteristics and preparation process, potential impact on the quality of peptide drugs, etc., we carry out perfect impurity profiling research and control to ensure the effectiveness and safety of peptide drugs. Semaglutide side chain and Tirzepatide side chain had completed the process verification (90kg) and accumulated dozens of batches, the quality between batches is stable, and the impurity spectrum is consistent.



Chromatogram 1 Multi-batch superposition chromatogram of Tirzepatide side chain



Chromatogram 2 Multi-batch superposition chromatogram of Semaglutide side chain

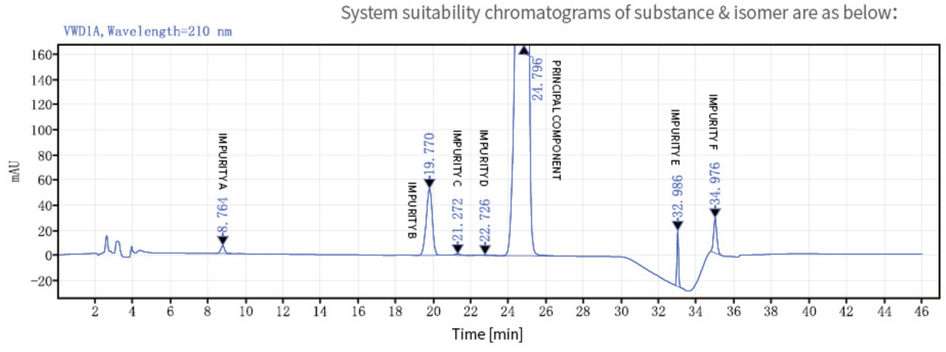
SHORT PEPTIDE PLATFORM

Using certain short peptide fragments as starting materials is one of the ways to chemically synthesize peptides. Compared with protecting amino acids, using short peptide fragments as starting materials can shorten the production cycle, effectively control some specific impurities, and is an effective means to deal with difficult-to-synthesize sequences. Pukang has established a short peptide platform to assist the development and industrialization of new peptide drugs, including the following categories:

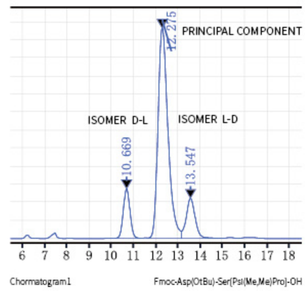
SEMAGLUTIDE SHORT PEPTIDE | TIRZEPATIDE SHORT PEPTIDE | PSEUDODIPEPTIDE | OTHER CUSTOMIZED SHORT PEPTIDES

The short peptides in the Pukang platform have all completed pharmacological studies in accordance with the requirements of ICH M4, and the impurity profiles have been systematically studied and controlled, and 100-kilogram-scale production has been realized. The following is an example: Boc-His(Trt)-Aib-Glu(OtBu)-Gly-OH (CAS: 1890228-73-5)

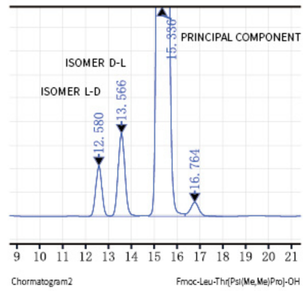
System suitability chromatograms of substance & isomer are as below:



Pseudodipeptide series are the key research products of Pukang short peptide platform. The Pro-like structure formed in pseudodipeptide cannot form hydrogen bond, which can effectively inhibit the formation of β-fold, reduce aggregation and increase solubility, so that many difficult-to-synthesize sequences are no longer a problem. Below are some of the product isomer system suitability chromatograms:



Chromatogram1 Fmoc-Asp(OtBu)-Ser[Psi(Me,Me)Pro]-OH



Chromatogram2 Fmoc-Leu-Thr[Psi(Me,Me)Pro]-OH

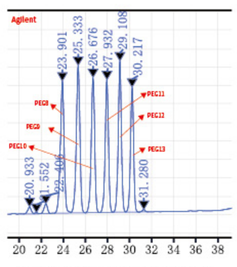
MONODISPERSE PEG DERIVATIVES PLATFORM

Polyethylene glycol (PEG) is a synthetic, hydrophilic, biocompatible, non-toxic, and immunogenic polymer used for drug modification. PEG modification technology has the following advantages:

- Enhance stability and extend drug half-life.
- Improve pharmacodynamic properties and reduce known toxicity.
- Improve solubility of insoluble drugs.
- Improve the distribution of drugs in the body, improve pharmacokinetic properties.

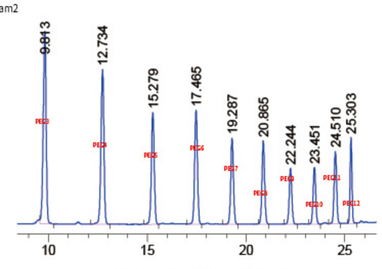
Monodisperse PEG, the molecular weight is clear, is a single compound, compared to polydisperse PEG has obvious advantages. According to the requirements of ICHQ3A and ICHQ11, the impurity spectrum control of monodisperse PEG derivatives is one of the important evidences to fully demonstrate the effectiveness and safety of drugs. The monodisperse PEGs supplied by Pukang all have strict control over their congeners:

Chormatogram1



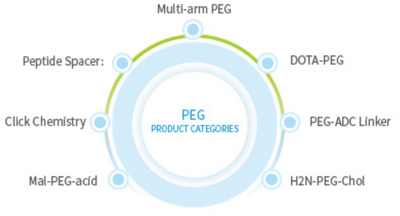
Protect-PEG series homologue separation

Chormatogram2



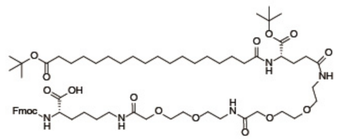
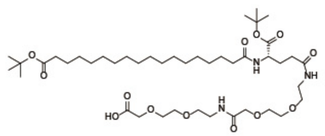
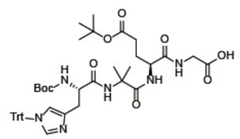
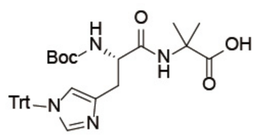
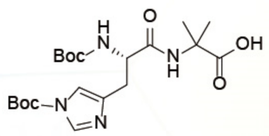
Separation of N3-PEG series homologs

The introduction of different end groups of PEG materials can give PEG excellent properties. At present, monodisperse PEG derivatives are used in the fields of peptide, XDC (ADC/RDC/PDC)-Linker, drug delivery and so on. According to the different end groups, Pukang has designed and prepared many series of PEG derivatives, and most of the products have been realized to be produced in 10 kg. We can also customize and assist in the design of different types of PEG derivatives upon request.



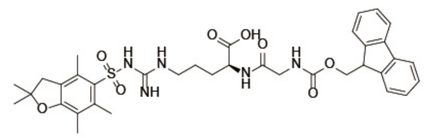
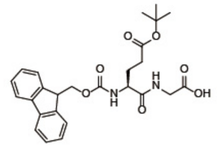
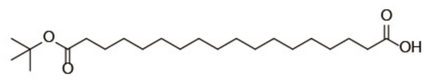
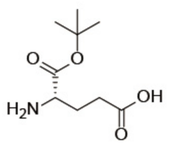
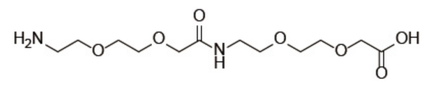
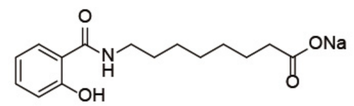
PUKANG
BIOTECHNOLOGY 普康生物科技

司美格鲁肽中间体
SEMAGLUTIDE INTERMEDIATES

CAS No.	Chemical Structure/ Product Name	Quality Index
1662688-20-1	 Fmoc-Lys(Oct-(OtBu)-γ-Glu(OtBu)-AEEA-AEEA)-OH	DMF No.: 039906
1118767-16-0	 tBuO-Ste-Glu(AEEA-AEEA-OH)-OtBu	DMF No.: 040151
1169630-40-3	Ste-Glu-AEEA-AEEA-OSU	Complete set of CMC research document
1890228-73-5	 Boc-His(Trt)-Aib-Glu(OtBu)-Gly-OH	Complete set of CMC research document
2061897-68-3	 Boc-His(Trt)-Aib-OH	Complete set of CMC research document
1169630-98-1	 Boc-His(Boc)-Aib-OH	Complete set of CMC research document

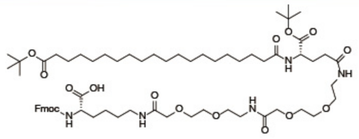
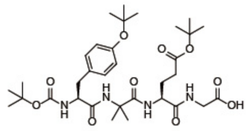
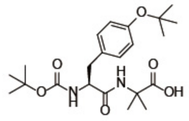
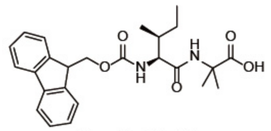
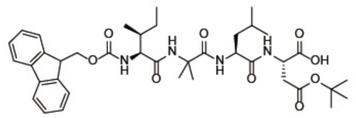
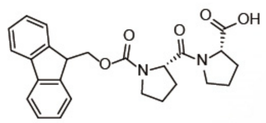
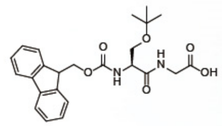
司美格鲁肽中间体
SEMAGLUTIDE INTERMEDIATES

普康 PUKANG

CAS No.	Chemical Structure/ Product Name	Quality Index
1048377-78-1	 Fmoc-Gly-Arg(Pbf)-OH	Single impurity ⩽0.2%
866044-63-5	 Fmoc-Glu(OtBu)-Gly-OH	Single impurity ⩽0.1%
843666-40-0	 18-(tert-butoxy)-18-oxooctadecanoic acid	Homologous impurities ⩽0.1%
45120-30-7	 1-OtBu-L-Glu	Complete impurity profile study
1143516-05-5	 AEEA-AEEA	Complete impurity profile study
203787-91-1	 SNAC	DMF No.: 39196 CDE No.: F20240000152

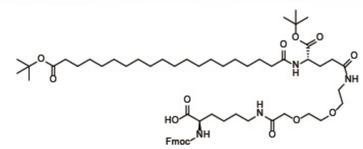
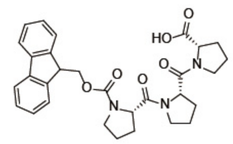
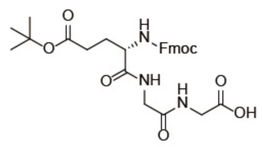
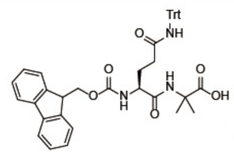
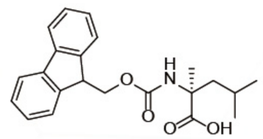
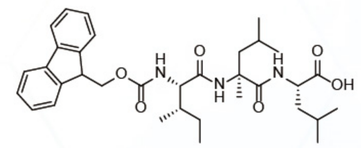
PUKANG
BIOTECHNOLOGY 普康生物科技

替尔泊肽中间体
TIRZEPATIDE INTERMEDIATES

CAS No.	Chemical Structure/ Product Name	Quality Index
2915356-76-0	 Fmoc-Lys[AEEA-AEEA -γ -Glu(OtBu)-C20-OtBu]-OH	DMF No.: 039989
2682040-93-1	 Boc-Tyr(tBu)-Aib-Glu(OtBu)-Gly-OH	Complete set of CMC research document
2639221-78-4	 Boc-Tyr(tBu)-Aib-OH	Complete set of CMC research document
2171139-20-9	 Fmoc-Ile-Aib-OH	Purity ⩾99% Single impurity ⩽0.2%
2915356-38-4	 Fmoc-Ile-Aib-Leu-Asp(OtBu)-OH	Purity ⩾99% Single impurity ⩽0.2%
129223-22-9	 Fmoc-Pro-Pro-OH	Purity ⩾99% Single impurity ⩽0.2%
81672-17-5	 Fmoc-Ser(tBu)-Gly-OH	Purity ⩾99% Single impurity ⩽0.2%

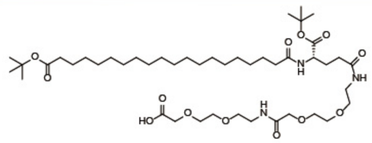
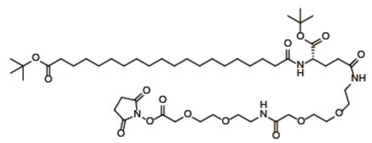
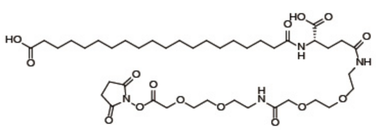
瑞他鲁肽中间体
RETATRUTIDE INTERMEDIATES

普康
PUKANG

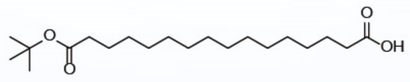
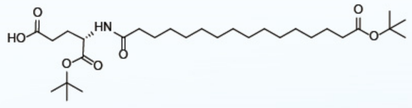
CAS No.	Chemical Structure/ Product Name	Quality Index
2612237-97-3	 Fmoc-Lys[C20-OtBu-γ-Glu(OtBu)-AEEA] -OH	Complete impurity profile study
134303-96-1	 Fmoc-Pro-Pro-Pro-OH	Purity ⩾98.0%
NA	 Fmoc-Glu(OtBu)-Gly-Gly-OH	Complete impurity profile study
NA	 Fmoc-Gln(Trt)-Aib-OH	Purity ⩾98.0%
312624-65-0	 Fmoc-α-Me-Leu-OH	Purity ⩾99.0%
NA	 Fmoc-Ile-α-Me-Leu-Leu-OH	Purity ⩾99.0%

PUKANG
BIOTECHNOLOGY 普康生物科技

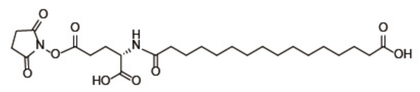
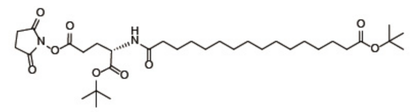
超长效胰岛素中间体
INSULIN ICODEC INTERMEDIATES

CAS No.	Chemical Structure/ Product Name	Quality Index
1188328-37-1	 tBuO-C20-Glu(AEEA-AEEA)-OH-OtBu	Complete set of CMC research document
NA	 tBuO-C20-Glu(OtBu)-AEEA-AEEA-OSU	Purity ⩾98.0%
1188328-38-2	 C20-Glu-AEEA-AEEA-OSU	Complete set of CMC research document

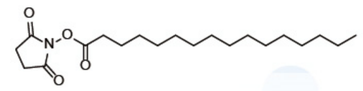
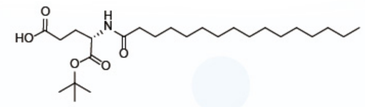
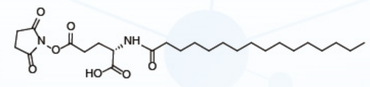
德谷胰岛素中间体
INSULIN DEGLUDEC INTERMEDIATES

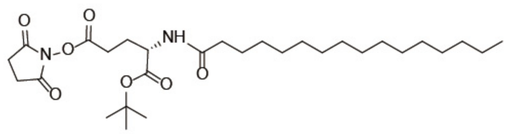
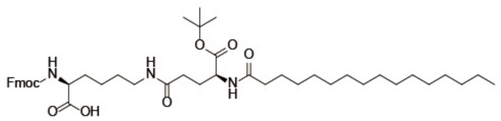
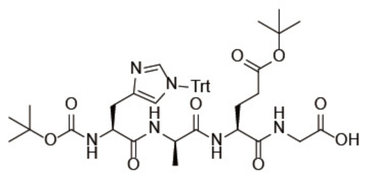
CAS No.	Chemical Structure/ Product Name	Quality Index
843666-27-3	 16-(Tert-butoxy)-16-oxohexadecanoic acid	Complete impurity profile study
843666-29-5	 C16-OtBu-Glu(OH)-OtBu	Purity ⩾95.0%

德谷胰岛素中间体
INSULIN DEGLUDEC INTERMEDIATES

CAS No.	Chemical Structure/ Product Name	Quality Index
943586-12-7	 HO-C16-Glu(OSU)-OH	Purity ⩾90.0%
843666-26-2	 tBuO-C16-Glu(OSU)-OtBu	Complete set of CMC research document

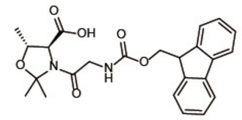
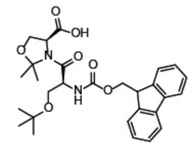
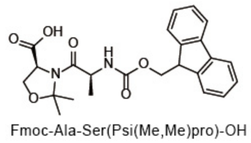
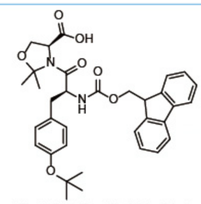
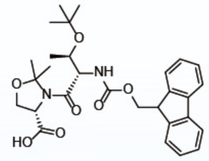
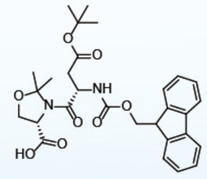
利拉鲁肽中间体
LIRAGLUTIDE INTERMEDIATES

CAS No.	Chemical Structure/ Product Name	Quality Index
14464-31-4	 Pal-OSU	Purity ⩾98.0%
536721-25-2	 Pal-Glu-OtBu	Complete impurity profile study
294855-91-7	 Pal-Glu(OSu)-OH	Purity ⩾98.0%

CAS No.	Chemical Structure/ Product Name	Quality Index
204521-63-1	 Pal-Glu(OSu)-OtBu	Isomer Impurities ⩽0.1%
1491158-62-3	 Fmoc-Lys(Pal-Glu-OtBu)-OH	Complete set of CMC research document
1418291-58-3	 Boc-His(Trt)-Ala-Glu(OtBu)-Gly-OH	Complete impurity profile study

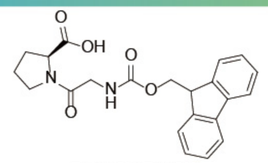
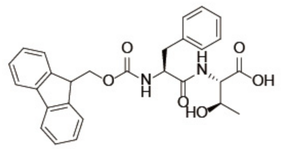
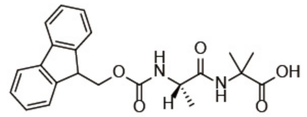
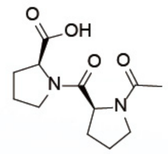
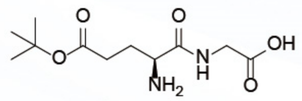
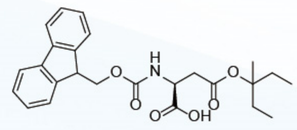
伪二肽
PSEUDODIPEPTIDES

The introduction of chemically modified peptide chain temporarily destroys the advanced structure of “difficult sequence” peptide and promotes peptide solubilization, thus facilitating the synthesis of peptide. For example, when the peptide chain contains a proline fragment, the amide bond formed by condensation does not have a proton that can form a hydrogen bond, and the α-carbon atom of the proline is in the rigid structure of the five-membered ring, which inhibits the formation of the β-folding structure. Therefore, when synthesizing the long peptide sequences, a pseudoproline dipeptide structure is introduced to improve the aggregation and promote the synthesis. After the peptide chain is assembled on the resin, the peptide is cleaved from the resin by acidic reagent, and the normal sequence is restored without affecting the properties of the peptide.

CAS No.	Chemical Structure/ Product Name	Quality Index
1262308-49-5	 Fmoc-Gly-Thr(Psi(Me,Me)pro)-OH	Complete impurity profile study
1000164-43-1	 Fmoc-Ser(tBu)-Ser(Psi(Me,Me)pro)-OH	Complete impurity profile study
252554-78-2	 Fmoc-Ala-Ser(Psi(Me,Me)pro)-OH	Complete impurity profile study
878797-09-2	 Fmoc-Tyr(tBu)-Ser(Psi(Me,Me)pro)-OH	Complete impurity profile study
1425938-63-1	 Fmoc-Thr(tBu)-Ser(Psi(Me,Me)pro)-OH	Complete impurity profile study
955048-92-7	 Fmoc-Asp(OtBu)-Ser(Psi(Me,Me)pro)-OH	Complete impurity profile study

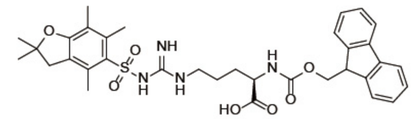
PUKANG
BIOTECHNOLOGY 普康生物科技

其它短肽
OTHER SHORT PEPTIDES

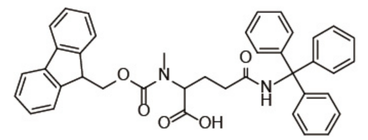
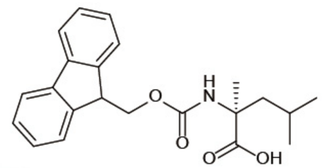
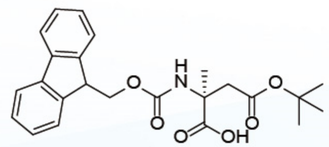
CAS No.	Chemical Structure/ Product Name	Quality Index
212651-48-4	 Fmoc-Gly-Pro-OH	Complete impurity profile study
87720-57-8	 Fmoc-Phe-Thr-OH	Purity ⩾98.5%
107076-70-0	 Fmoc-β-Ala-Aib-OH	Max unknown single impurity ⩽0.1% Purity ⩾98%
202470-30-2	 Ac-Pro-Pro-OH	Complete impurity profile study
23406-82-8	 H-Glu(OtBu)-Gly-OH	Isomer Impurities ⩽0.1% Purity ⩾98.5%
180675-08-5	 Fmoc-Asp(Ompe)-OH	Isomer Impurities ⩽0.15% Purity ⩾98.5%

其它短肽
OTHER SHORT PEPTIDES

普康 PUKANG

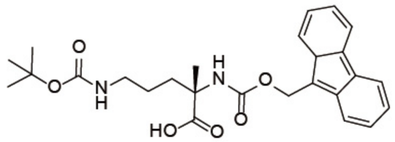
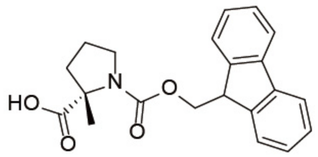
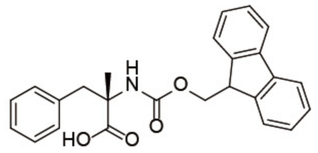
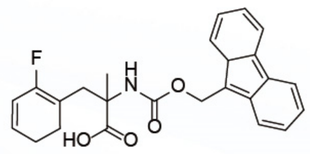
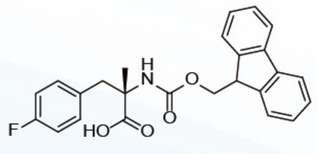
CAS No.	Chemical Structure/ Product Name	Quality Index
187618-60-6	 Fmoc-D-Arg(Pbf)-OH	Complete impurity profile study

非天然氨基酸
UN-NATURAL AMINO ACIDS

CAS No.	Chemical Structure/ Product Name	Quality Index
1632075-13-8	 Fmoc-N-Me-Gln(Trt)-OH	Purity ⩾98.0%
312624-65-0	 Fmoc-α-Me-L-Leu-OH	Purity ⩾98.5%
1072845-47-6	 Fmoc-α-Me-Asp(OtBu)-OH	Purity ⩾98.0%

PUKANG
BIOTECHNOLOGY 普康生物科技

非天然氨基酸
UN-NATURAL AMINO ACIDS

CAS No.	Chemical Structure/ Product Name	Quality Index
171860-40-5	 Fmoc-α-Me-D-Orn(Boc)-OH	Purity ⩾97.0%
167275-47-0	 Fmoc-α-Me-Pro-OH	Purity ⩾98.5%
135944-05-7	 Fmoc-α-Me-Phe-OH	Purity ⩾98.0%
1172127-44-4	 Fmoc-α-Me-L-2-Fluorophe-OH	Purity ⩾98.0%
1217777-84-8	 Fmoc-α-Me-D-Phe(4-F)-OH	Purity ⩾98.0%

PEG 衍生物
PEG DERIVATIVES

普康
PUKANG

Controlling impurities in PEG derivatives is essential for demonstrating drug safety and efficacy. Homologous impurity is a critical quality attribute of monodisperse PEG and a key focus in drug evaluation. Pukang's PEG products maintain low content of homologous impurities, enhancing drug quality and supporting regulatory submissions.

PEG category	Product name	Quality Index
Protect PEG	Fmoc-NH-PEGn-CH2COOH Fmoc-NH-PEGn-CH2CH2COOH Fmoc-NH-PEGn-CH2CH2COONHS Boc-NH-PEGn-CH2COOH Boc-NH-PEGn-CH2CH2COOH Cbz-NH-PEGn-CH2COOH Cbz-NH-PEGn-CH2CH2COOH	n⩽24 Purity ⩾99.0% Homologous impurities ⩽0.2%(n⩽12) Homologous impurities ⩽0.4%(n⩽24)
Amino PEG	NH2-PEGn-CH2COOH NH2-PEGn-CH2OOtBu NH2-PEGn-CH2CH2COOH NH2-PEGn-CH2CH2COOtBu	
Azide PEG	N3-PEGn-OH N3-PEGn-NH2 N3-PEGn-CH2COOH N3-PEGn-CH2CH2COOH N3-PEGn-CH2CH2NH2 N3-PEGn-CH2CH2Br	
Allylene PEG	Allylene-PEGn-OH Allylene-PEGn-CH2COOH Allylene-PEGn-CH2COOtBu Allylene-PEGn-CH2CH2COOH Allylene-PEGn-CH2CH2COOtBu	n⩽36 Purity ⩾99.0%

PUKANG
BIOTECHNOLOGY 普康生物科技

PEG 衍生物
PEG DERIVATIVES

PEG category	Product name	Quality Index
DBCO PEG	DBCO-PEGn-MAL DBCO-PEGn-NHS ester DBCO-PEGn-DBCO DBCO-NHCO-PEGn-maleimide	n≤24 Purity ≥98.0%
Methyl ether PEG	Methyl ether-PEGn-OH Methyl ether-PEGn -Br Methyl ether-PEGn-CH2COOH Methyl ether-PEGn-CH2CH2COOH Methyl ether-PEGn -CH2CH2COONHS	n≤24 Purity ≥98.0%
Maleimide-PEG	Maleimide-PEGn-CH2COOH Maleimide-PEGn-CH2CH2COOH Maleimide-PEG-CH2CH2COONHS	n≤24 Purity ≥98.0% Homologous impurities ≤0.5%
Arms PEG	NH-Bis(PEGn-azide) NH-bis(PEGn-Boc) NH-bis(PEGn-acid) NH-bis(PEGn-C2-NH-Boc) N-(Azido-PEGn)-N-bis(PEGn-NHS ester) N-(Amino-PEGn)-N-bis(PEGn-azide)	n≤24 Purity ≥98.0%

普康 PUKANG

OUR MANAGEMENT SYSTEM

Pukang has established a good management system based on international advanced concepts and regulations to ensure the standardization of production and operation activities. This includes a quality management system based on China GMP2010 and ICH Q7, and an EHS management system based on relevant regulations.

EXCELLENT QUALITY SYSTEM AND EHS MANAGEMENT SYSTEM ARE THE GUARANTEE OF STABLE SUPPLY OF PRODUCTS.